**B**

Competitor	-		DE wt		DE m1		DE m2		DE m3		ARE				
Activin injected	-	-	+	-	-	+	-	-	+	-	-	+	-	-	+
Embryo stage	St8 St11		St8 St11		St8 St11		St8 St11		St8 St11		St8 St11		St8 St11		

DEBP →

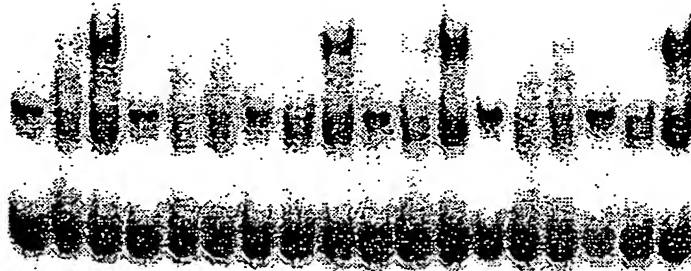


Figure 1

Probe

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

DE wt → ← ←

CATTAATCAGATTAACGGTGAGCAATTAG

DE m1 --G-C-G---C-G-C-----

DE m2 --G-C-----G-C-----G-C-

DE m3 -----TTGT-----G---

C

Embryo stage	St 8		St 10.5		
Cycloheximide	-	-	+	-	+
Activin injected	-	-	-	+	+

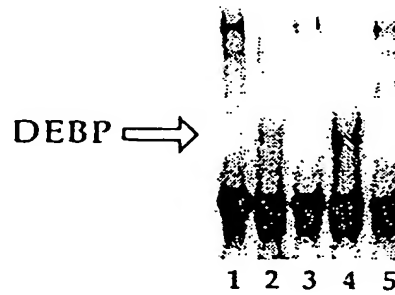
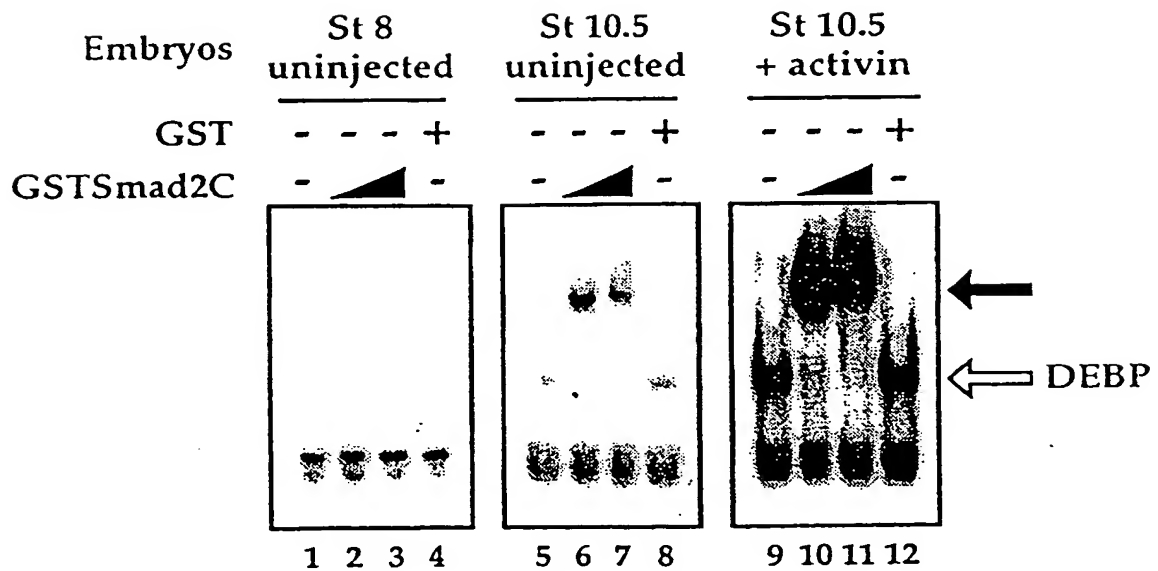
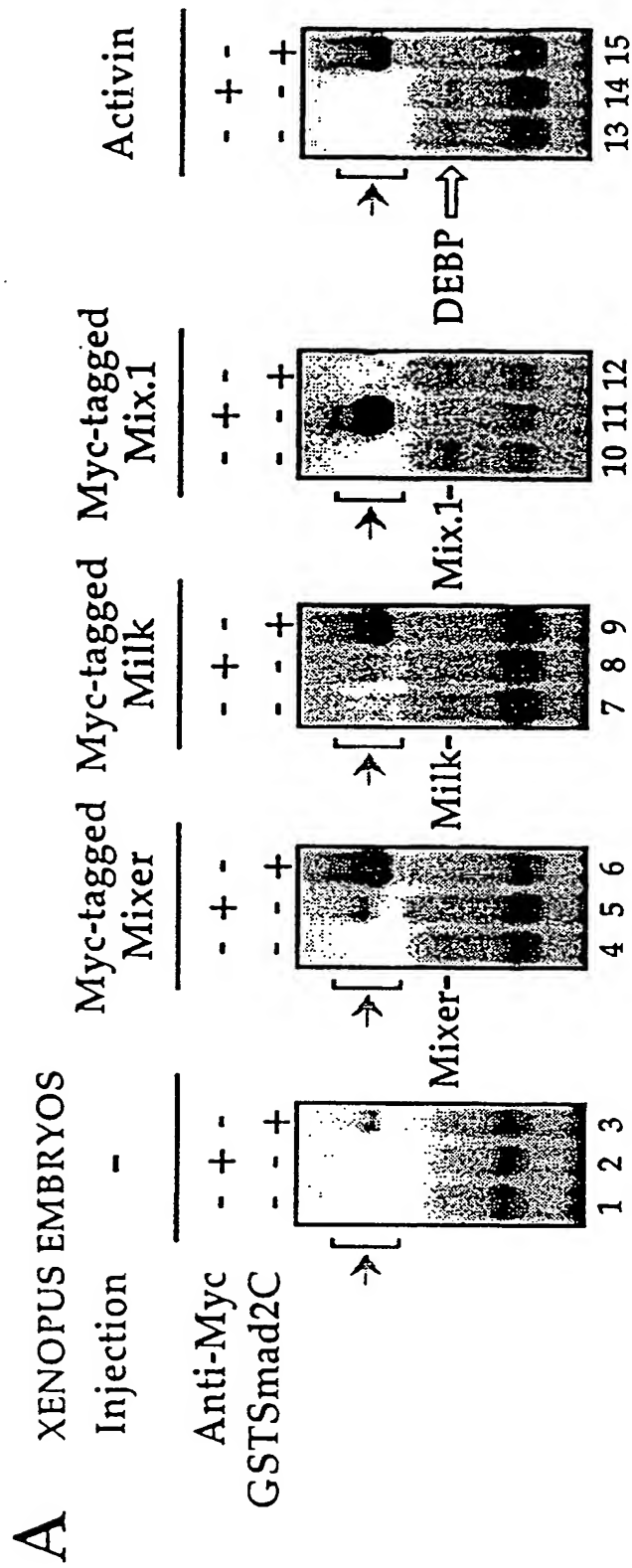


Figure 1

Figure 2





B IN VITRO-TRANSLATED

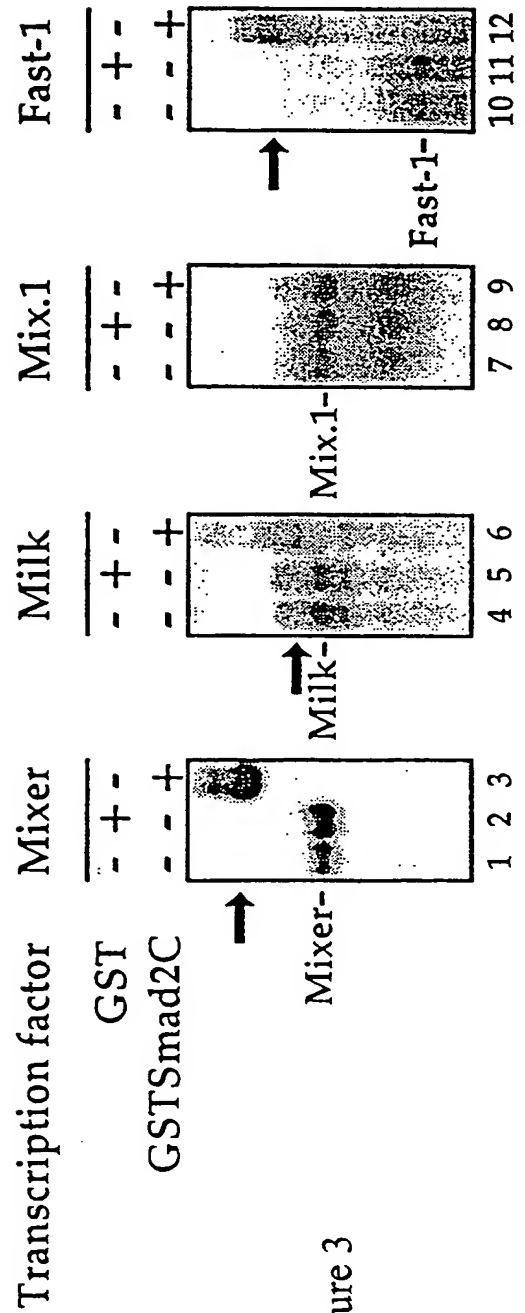
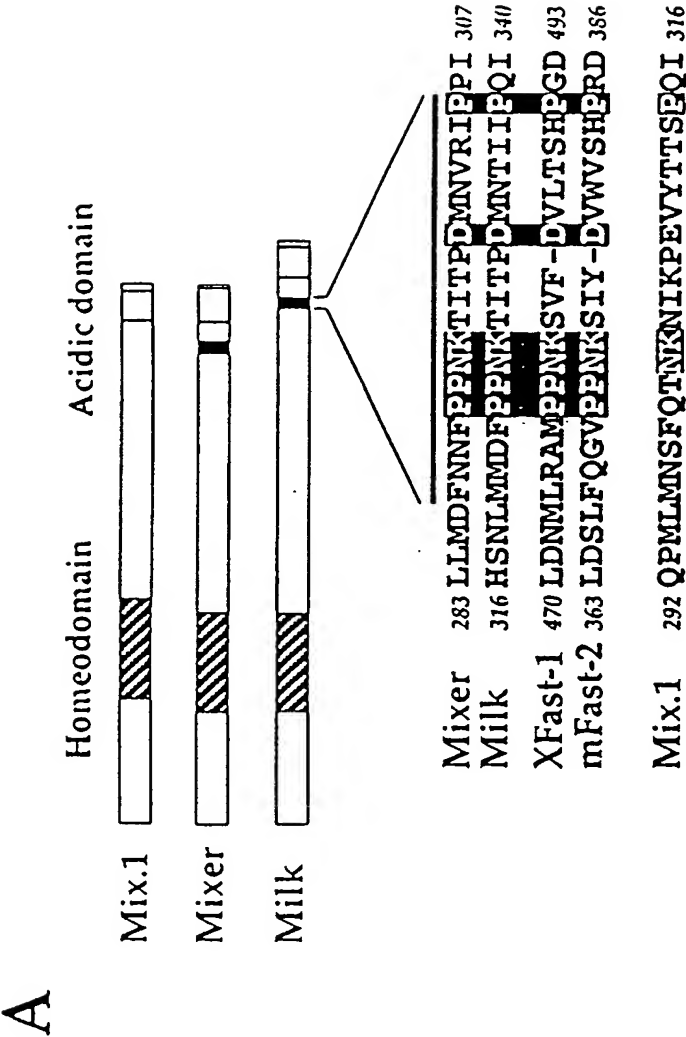


Figure 3



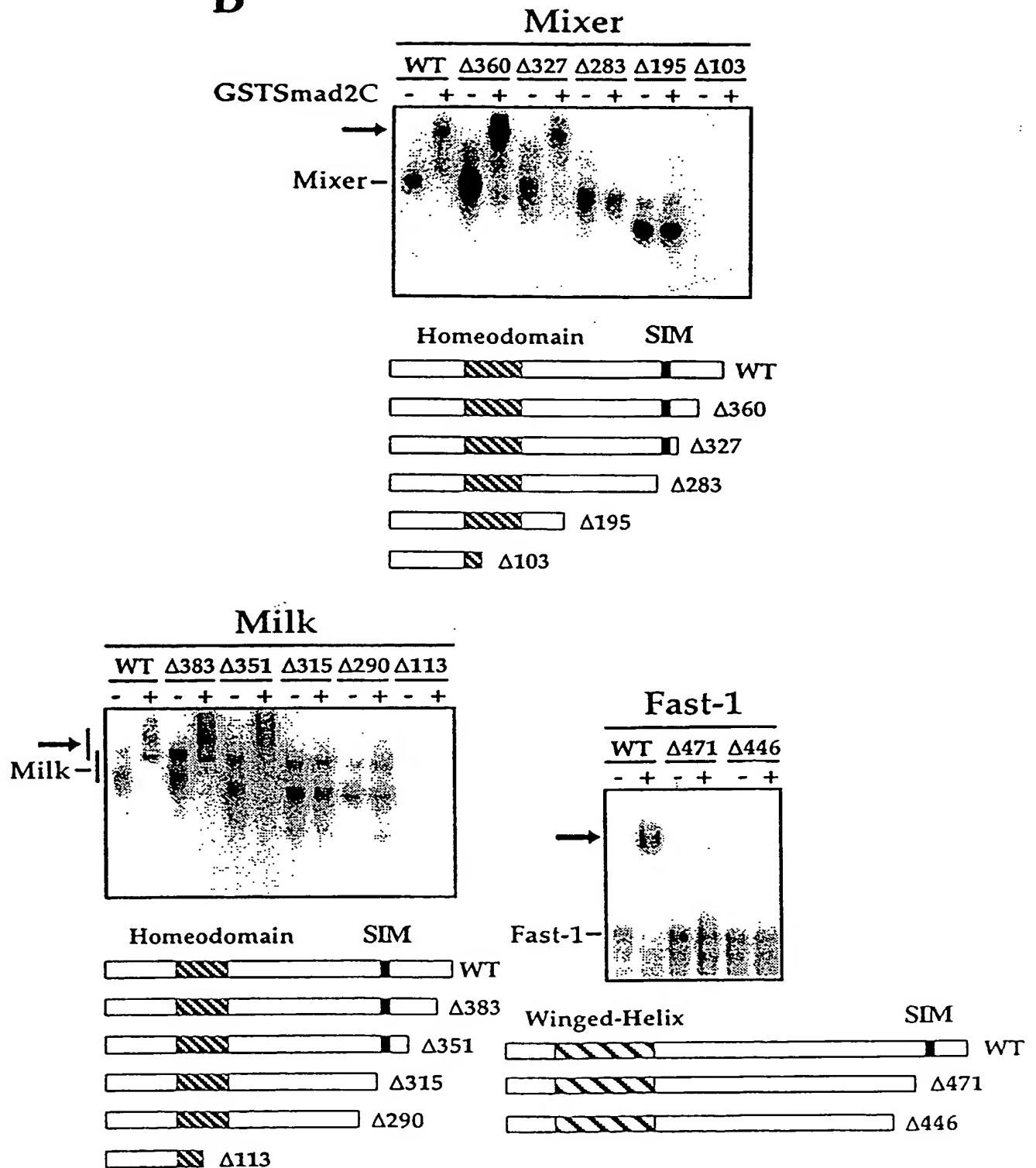
B

Figure 4

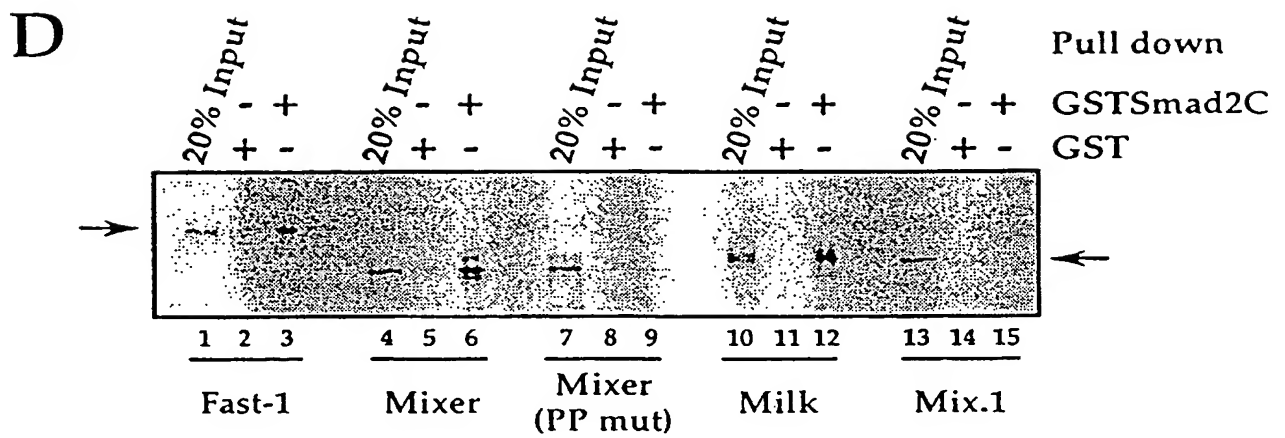
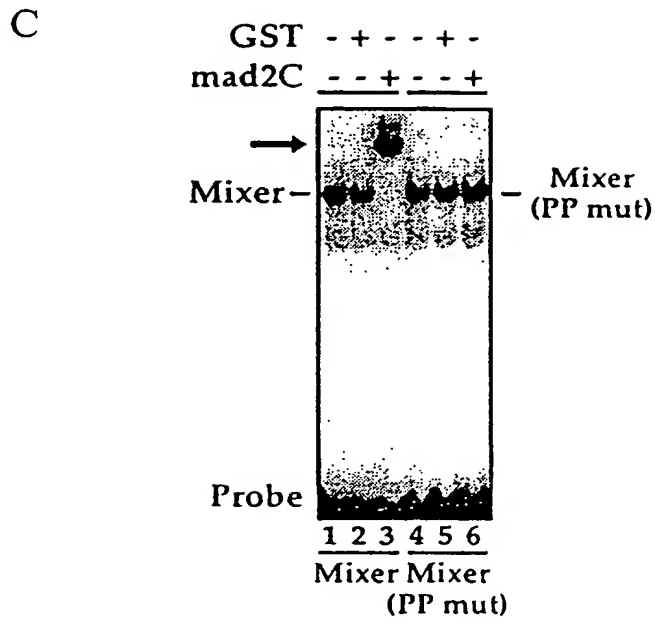


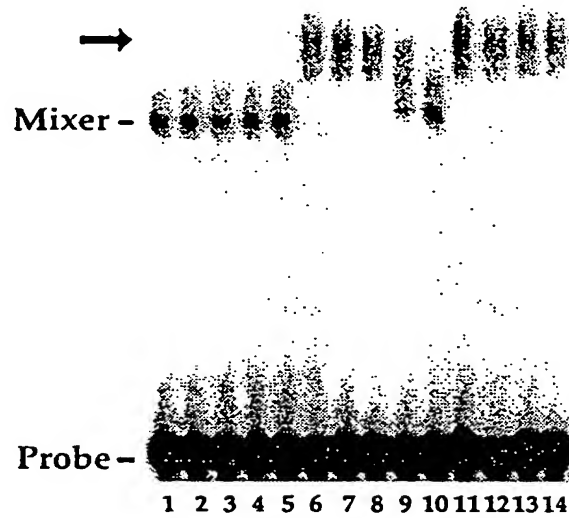
Figure 4

6/30

A

Probe: DE
Protein: Mixer

GSTSmad2C	-		+	
Competing peptide	WT	Mut	WT	Mut
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	0	0	0	0
6	0	0	0	0
7	0	0	0	0
8	0	0	0	0
9	0	0	0	0
10	0	0	0	0
11	0	0	0	0
12	0	0	0	0
13	0	0	0	0
14	0	0	0	0
15	0	0	0	0
16	0	0	0	0
17	0	0	0	0
18	0	0	0	0
19	0	0	0	0
20	0	0	0	0
21	0	0	0	0
22	0	0	0	0
23	0	0	0	0
24	0	0	0	0
25	0	0	0	0
26	0	0	0	0
27	0	0	0	0
28	0	0	0	0
29	0	0	0	0
30	0	0	0	0
31	0	0	0	0
32	0	0	0	0
33	0	0	0	0
34	0	0	0	0
35	0	0	0	0
36	0	0	0	0
37	0	0	0	0
38	0	0	0	0
39	0	0	0	0
40	0	0	0	0
41	0	0	0	0
42	0	0	0	0
43	0	0	0	0
44	0	0	0	0
45	0	0	0	0
46	0	0	0	0
47	0	0	0	0
48	0	0	0	0
49	0	0	0	0
50	0	0	0	0
51	0	0	0	0
52	0	0	0	0
53	0	0	0	0
54	0	0	0	0
55	0	0	0	0
56	0	0	0	0
57	0	0	0	0
58	0	0	0	0
59	0	0	0	0
60	0	0	0	0
61	0	0	0	0
62	0	0	0	0
63	0	0	0	0
64	0	0	0	0
65	0	0	0	0
66	0	0	0	0
67	0	0	0	0
68	0	0	0	0
69	0	0	0	0
70	0	0	0	0
71	0	0	0	0
72	0	0	0	0
73	0	0	0	0
74	0	0	0	0
75	0	0	0	0
76	0	0	0	0
77	0	0	0	0
78	0	0	0	0
79	0	0	0	0
80	0	0	0	0
81	0	0	0	0
82	0	0	0	0
83	0	0	0	0
84	0	0	0	0
85	0	0	0	0
86	0	0	0	0
87	0	0	0	0
88	0	0	0	0
89	0	0	0	0
90	0	0	0	0
91	0	0	0	0
92	0	0	0	0
93	0	0	0	0
94				



B

Probe: ARE
Protein: Embryo extract

Competing peptide

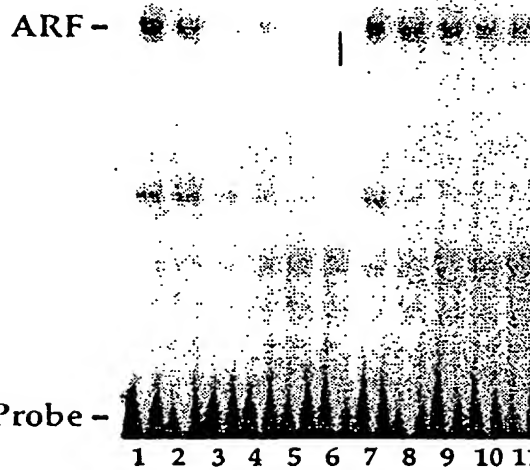
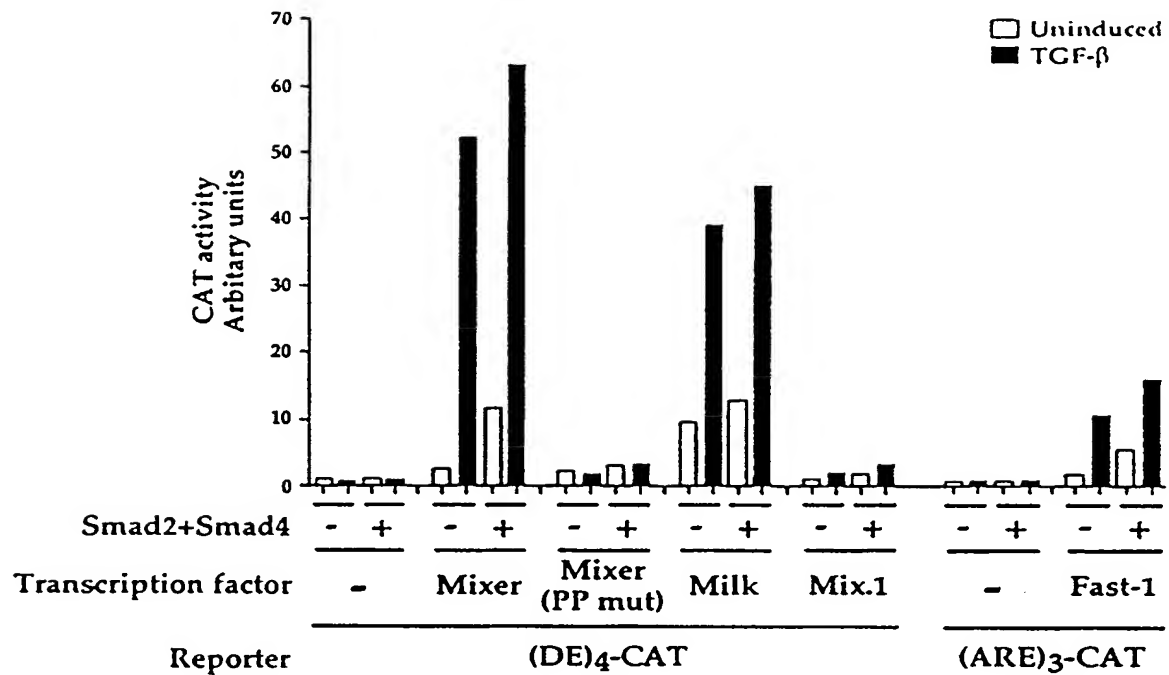


Figure 5

A



B

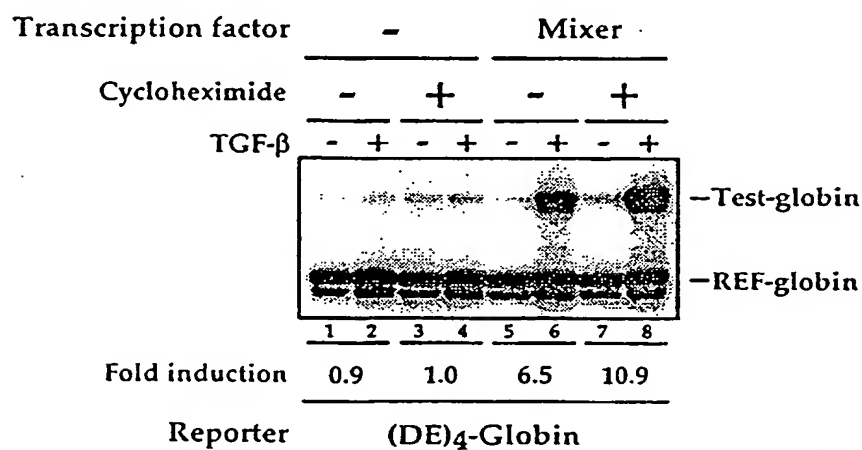


Figure 7

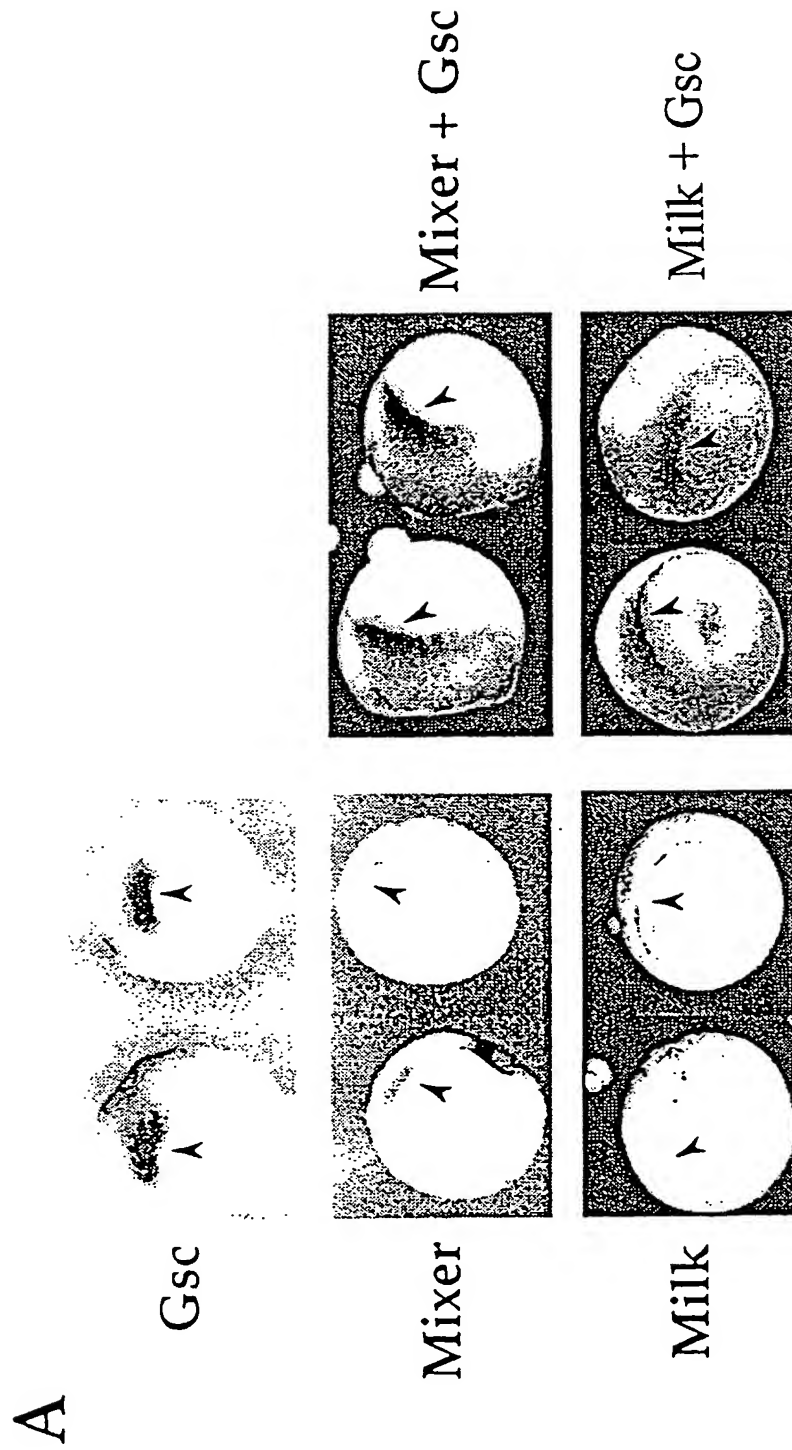


Figure 8

B

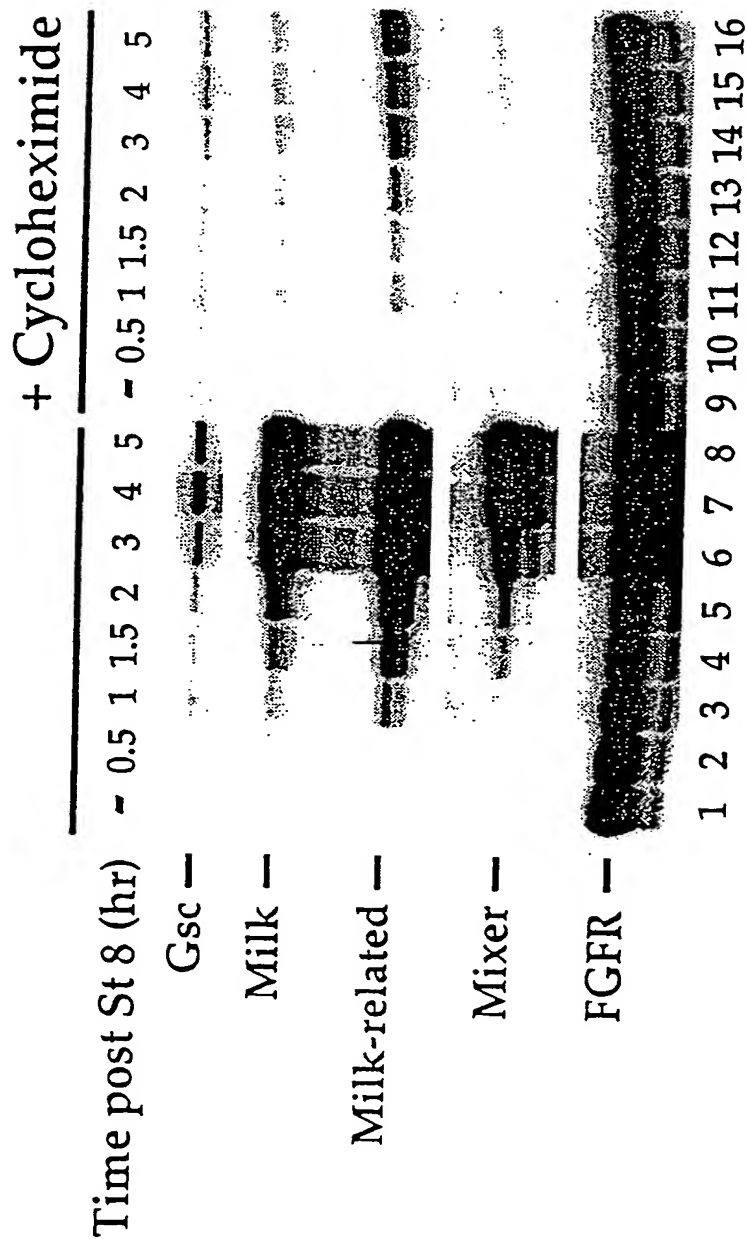


Figure 8

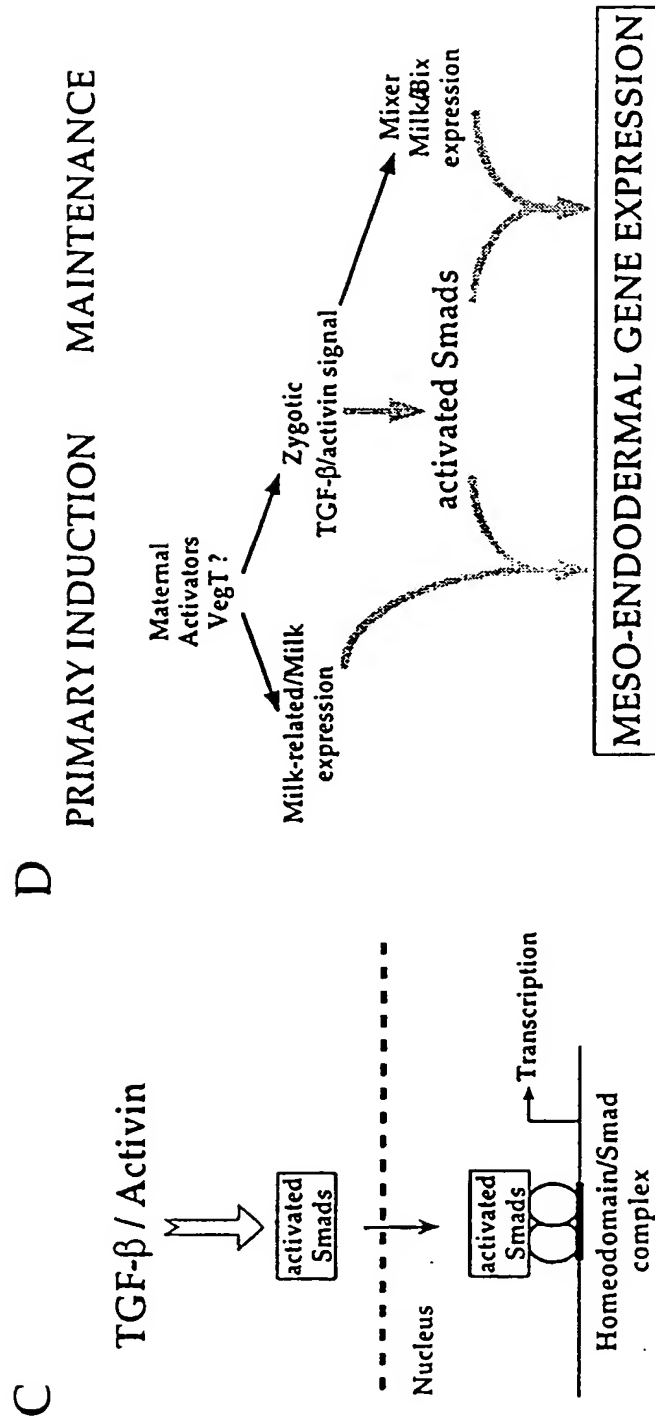


Figure 8

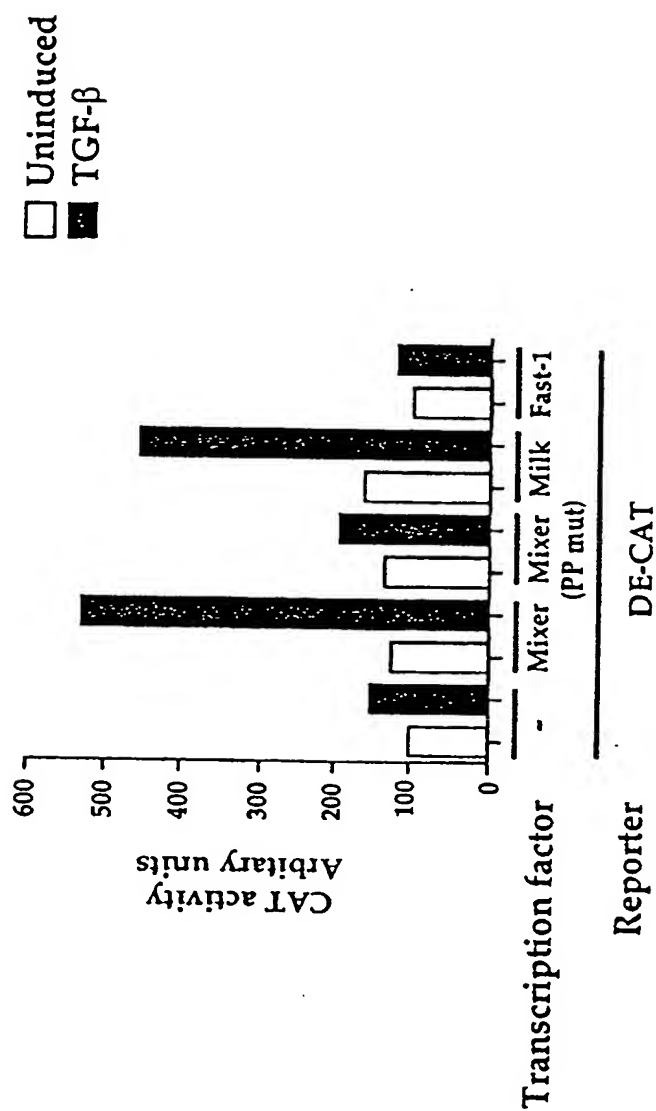


Figure 9

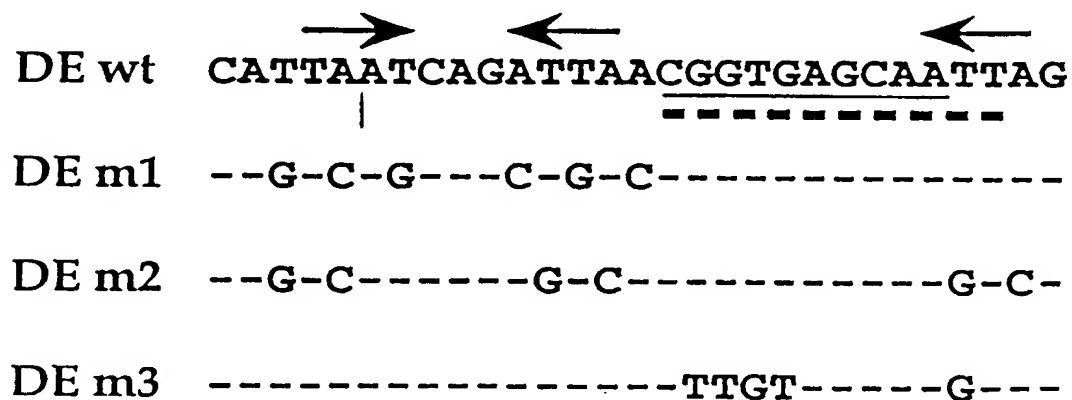
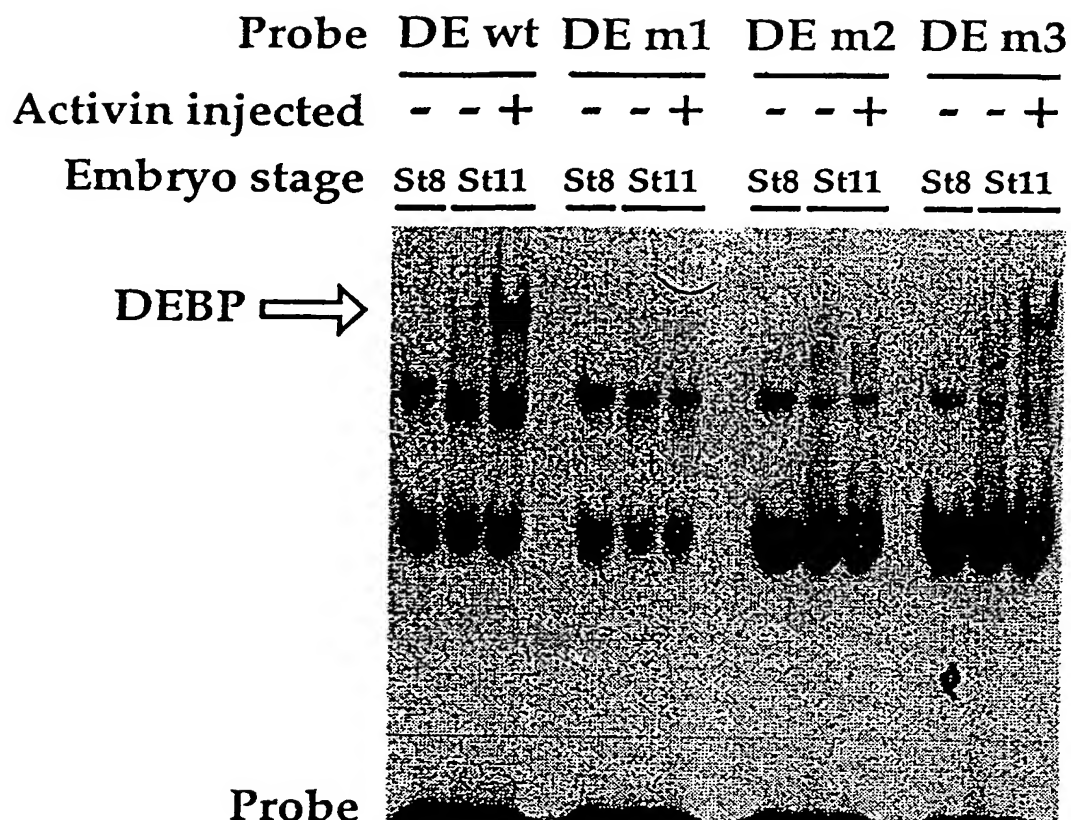


Figure 10

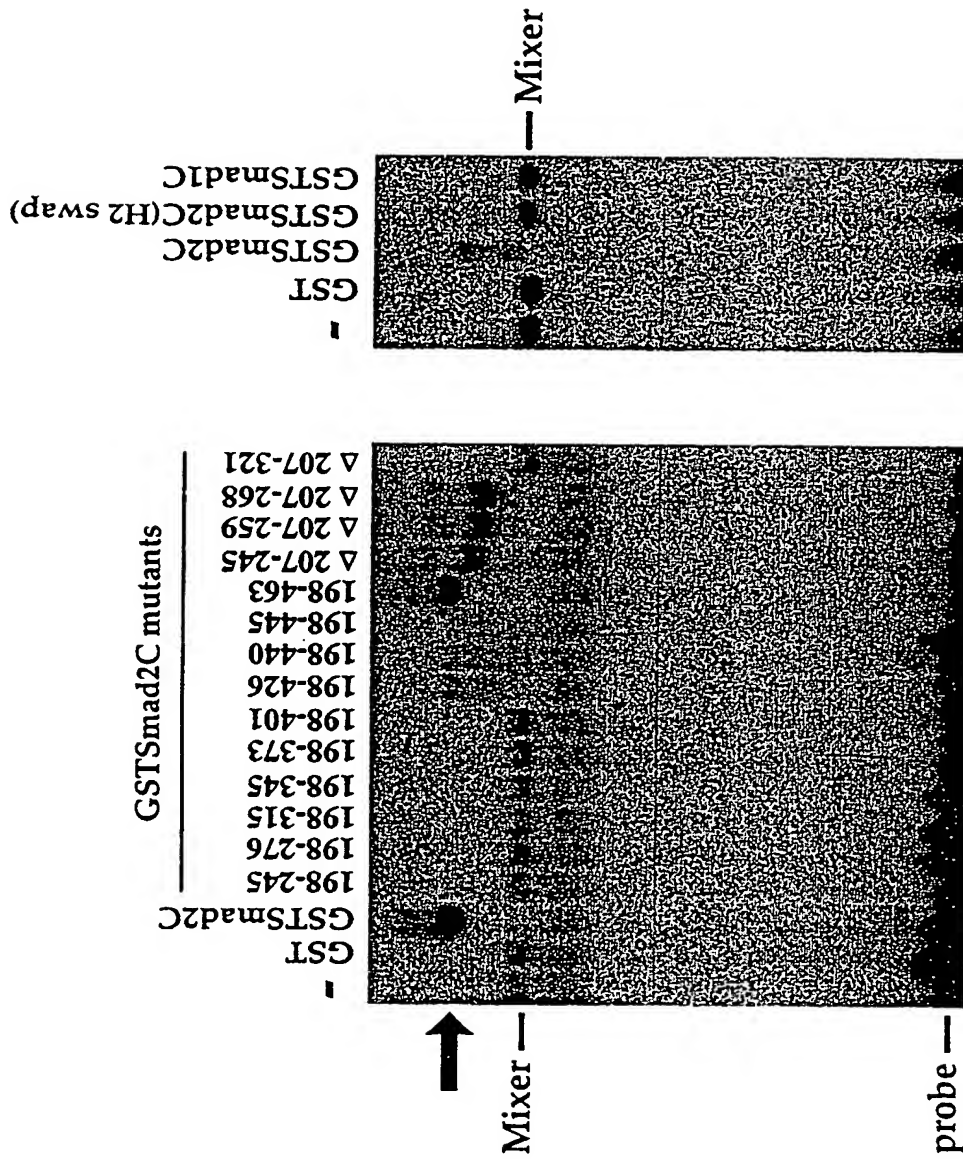


Figure 11

XSmad2

MAGSMSSILPFTPPVVKRLLGWKKASGTTGAGGDEQNGQEEKWCEKAVK
 SLVKKLKKTGQLELEKAITTQNCNTKCVTIPTCSEIWGLSTANTIDQW
 DTTGLYSFSEQTRSLDGRQLQVSHRKGLPHVIYCRLLWRWPDLSHSHHELKAI
 ENCEYAFNLKKDEVCVNPYHYQRVETPVLPPVLVPRHTEILTELPPLDDY
 THSIPENTNFPAGIEPQSNYIPETPPPGYISEDGETSDQQLNQSMGTGSP
 AELSPSTLSPVNHNLDLQPVTYSEPAFWCSIAYYELNQRVGETFFHASQPS
 LTVDGFTDPSNSERFCLGLLSNVNRNATVEMTRRHIGRGVRLYYIGGEVF
 AECLSDSAIFVQSPNCNQRYGWHPATVCKIPPGCNLKI FNNQEFALLAQ
 SVNQGFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHNLGPL
 QWLDKVLTMGSPSVRCSSMS

Hsmad2

MSSILPFTPPVVKRLLGWKKASGSGGAGGGEQNGQEEKWCEKAVKSLVK
 KLKKTGRLELEKAITTQNCNTKCVTIPTCSEIWGLSTPNTIDQWDTTG
 LYSFSEQTRSLDGRQLQVSHRKGLPHVIYCRLLWRWPDLSHSHHELKAIENCE
 YAFNLKKDEVCVNPYHYQRVETPVLPPVLVPRHTEILTELPPLDDYTHSI
 PENTNFPAGIEPQSNYIPETPPPGYISEDGETSDQQLNQSMGTGSPAELS
 PTTLSPVNHSLLDLQPVTYSEPAFWCSIAYYELNQRVGETFFHASQPSLTV
 GFTDPSNSERFCLGLLSNVNRNATVEMTRRHIGRGVRLYYIGGEVFAECL
 SDSAIFVQSPNCNQRYGWHPATVCKIPPGCNLKI FNNQEFALLAQSVNQ
 GFEAVYQLTRMCTIRMSFVKGWGAEYRRQTVTSTPCWIELHNLGPLQWLD
 KVLTMGSPSVRCSSMS

Figure 12

Xsmad3
 MSSILPFTPPPIVKRLLGWKKGEQNGQEEKWCEKAVKSLVKKLKKTGQLDE
 LEKALTTQSI STKCI TI PRSLDGR LQVSHRKGLPHVI YCRLWRWPD LSHH
 HELRAMEVCEYAFSMKKDEV CNPYHYQRVETPVLPPVLVPRNTEI PAEF
 PSLDDYSHSI PENTNFPAGIEPQIN YI PETPPPGYLS EDGETSDQMNH SI
 DTGSPNLSPNSMSPAHSNMDLQPVTYCEPAFWCSI SY YELNQRVGETFHA
 SQPSMTVDGFTDPSNSERFCLGLLSNVNRNAAVELTRRHIGRGVRLYYIG
 GEVFAECLSDNAIFVQSPNCNQRYGWHPATVCKI PPGCNLKI FNNQEEFAA
 LLAQSVNQGF EAVYQLTRMCTIRMSFVKGWGA EYRRQTVTSTPCWIELHL
 NGPLQWLDKVL TQMGSPSIRCSSVS

Hsmad3
 MSSILPFTPPPIVKRLLGWKKGEQNGQEEKWCEKAVKSLVKKLKKTGQLDE
 LEKAITTQNVNTKCI TI PRSLDGR LQVSHRKGLPHVI YCPVRWPD LSHH
 ELRAMELCEFAFMKKDEV CNPYHYQRVETPVLPPVLVPRHTEI PAEFP
 PLDDYSHSI PENTNFPAGIEPQSN I PETPPPGYLS EDGETSDHQMNH SMD
 AGSPNLSPNPMSPAHNNDLQPVTYCEPAFWCSI SY YELNQRVGETFFHAS
 QPSMTVDGFTDPSNSERFCLGLLSNVNRNAAVELTRRHIGRGVRLYYIGG
 EVFAECLSDSAIFVQSPNCNQRYGWHPATVCKI PPGCNLKI FNNQEEFAAL
 LLAQSVNQGF EAVYQLTRMCTIRMSFVKGWGA EYRRQTVTSTPCWIELHLN
 GPLQWLDKVL TQMGSPSIRCSSVS

Figure 12

301/1
 ATG TCC TCG ATA CTT CCC TTC ACT CCC CCC ATT GTC AAG AGG CTG TGG AAG AAG GGA GAG CAG AAC GGA
 M S S I L P F T P P I V K R L L G W K K G E Q N G
 331/11
 361/21
 391/31
 TGC GAG AAG GCA GTG AAA AGT CTG AAG AAG AGC GGC CAG CTG GAC GAG CTG GAG AAG GCA CTG
 C E K A V K S L V K K L K K S G Q L D E L E K A L
 451/51
 421/41
 481/61
 AGC ACC AAG TGC ATC ACC ATC CCC AGG TCT CTG GAT GGG AGA CTC CAG GTG TCC CAT CGT AAG GGG TTG CCT CAT
 S T K C I T I P R S L D G R L Q V S H R K G L P H
 541/81
 511/71
 571/91
 CTC TGG AGG TGG CCA GAT CTG CAC AGT CAC CAC GAG CTT CGA GCC ATG GAG GTG TGT GAA TAT GCC TTC AGC ATG
 L W R P D L H S H E L R A M E V C E Y A F S M
 601/101
 661/121
 TGT GTG AAT CCT TAT CAC TAC CAG AGA GTG GAG ACT CCA GTT CTA CCT CCT GTG CTG GTT CCA CGA AAC ACC GAA
 C V N P Y H Y Q R V E T P V L P V L V P R N T E
 721/141
 751/151
 OCT TCA CTT GAT GAT TAC AGC CAT TCC ATT CCG GAA AAT ACC AAT TTC CCA GCA GGC ATC GAG CCA CAG ACA AAC
 P S L D D Y S H S I P E N T N F P A G I E P Q I N
 811/171
 841/181
 CCT OCT CCC GGT TAC TTG AGC GAA GAT GGG GAA ACA AGC GAC CAA ATG AAT CAC AGT ATA GAT ACA GGC TCT CCA
 P P P G Y L S E D G E T S D Q M N H S I D T G S P
 901/201
 931/211
 TCT ATG TCT OCT GCT CAT AGC AAC ATG GAC CTG CAG CCT GTC ACA TAC TGC GAG CCG GCC TTT TGG TGT TCC ATC
 S M S P A H S N M D L Q P V T Y C E P A F W C S I
 991/231
 1021/241
 AAC CAA CGC GTA GGG GAG AGC TTC CAC GCT TCC CAG CCC TCC ATG ACA GTG GAT GGA TTC ACC GAT CCT TCC AAC
 N Q R V G E T F H A S Q P S M T V D G F T D P S N
 1081/261
 TCT GAA CGT TTC TGC
 S E R F C

Figure 12

1111/271 1141/281 1171/291
 CTG GGG CTG TTG TCC AAC GTA AAT CCG AAT GCA GCT GTG GAG CTG ACA CCG AGA CAC ATC GGG AGA GGC GTG CCG CTG
 L G L L S N V N R N A A V E L T R R H I G R G V R L
 TAT TAC ATT GGA
 1201/301 1231/311 1261/321 Y Y I G
 GGG GAA CTG TTT GCC GAG TGC CTC AGT GAC AAT GCC ATA TTT GTA CAG TCC CCA AAT TGT AAC CAG CCG TAC GGT TGG
 G E V F A E C L S D N A I F V Q S P N C N Q R Y G W
 CAT CCT GCC ACA
 1291/331 1321/341 1351/351 H P A T
 GTC TGC AAG ATT CCA CCA GGC TGT AAC CTG AAG ATA TTT AAT AAC CAG GAG TTT GCT GCT CTT TTG GCT CAG TCA GTA
 V C K I P P G C N L K I F N N Q E F A A L L A Q S V
 AAC CAG GGC TTT
 1381/361 1411/371 1441/381 N Q G F
 GAG GCT GTG TAT CAG CTT ACG AGG ATG TGC ACC ATA CGC ATG AGT TTC GTC AAA GGC TGG GGA GCC GAA TAC AGG CGA
 E A V Y Q L T R M C T I R M S F V K G A E Y R R
 CAG ACT GTG ACT
 1471/391 1501/401 1531/411 Q T V T
 AGC ACC CCC TGC TGG ATC GAG CTG CAC TTG AAC GGG CCC TTG CAA TGG TTG GAT AAG GTT CTC ACT CAG ATG GGG TCT
 S T P C W I E L H L N G P L Q W L D K V L T Q M G S
 CCA AGT ATC CCG
 P S I R
 1561/421
 TGC TCC AGT GTT TCT TAA
 C S S V S .

Figure 12

A

Mixer	KH-SQMPFHPSLLMDENNFPNKTITPDMNV--RIPPIPVSA PSNNHS
ZF Mixer	ANHAKSTMKQFLV-EYDNFFPNKTIGPEMKV--VIPPLPSQSNFMMSS
Milk	RH-NQVSMHSNLMMD <u>E</u> ---PPNKTITPDMNT--IIPQITDATGWSSQE
Bix3	RQ-NQVTMHSNLMVME <u>F</u> ---PPNKTITPDMNT--IIPQIPGATGWKNQE
XFast1	DSPRGPSPLDLDNMLRAMPPNKSVDVLT--SHPGDLVHPSFLSQC
HFast1	ETRGPPGLLCDLDALFQGVPPNKSIVDVWV--SHPRDLAAPGPGWLL
MFast2	ESQGSQDLLCDLDSLFQGVPPNKSIVDVWV--SHPRDLAAPGPGWLL
XFast3	PQIPLTPKPPPELKNAPSDFPNKTIVFDIPVYTGHPGFLASQSLFSPH

Figure 13

B

	Mixer SIM peptide	
Mixer	SQMPFHPSLLMDFNFPNKTITPDMNVRIPIPVSA PSNNH-	
ZF Mixer	AKSTMKQFL-VEYDNFPNKTIGPEMKVVIPLPSQSNFMMSS	
Milk	NQVSMHSNLMDF---PPNKTITPDMNTIIPQITDATGWS---	
Bix3	NQVTMHSNLVMEF---PPNKTITPDMNTIIPQIPGATGWK---	
Bix1	NQVSMHSNLMMDISNFPPTKTI TANMNTIIPQMPGASCWS---	
Bix4	NQVSMHSNIMMDFS NFQPKKTVTPDMNTIIPQIPDATGWS---	
Mix.1	QQMPVQPMMLNSF---QTNKNIKPEVYTTSPIPVSTTS----	
Mix.2	QQMPAQPMFMNSF---QTNKIIKSKMDTTSPPIPVSTTS SHH-	

SRMNVNTKEAGPLVSLPEDVYEE	371
SSPKHIACSVQNMSVQTQPELFAT	327
SQEGTDAYSTQGALPRAQCSPYGQ	400
NQEDINTYSTQGALSRAGCSSYGL	382
SHEDINAYSTQGAVPMAGCSPYGH	401
NQEGTDAYSTQEALPRAQCSPYGH	380
SQVSLFANQEPCHMSTTQGGTYGQ	377
SQMSLFAGQDPC HMSTAPGGTYGQ	369

Figure 13

C

XFast3

MSFGLHPWDVAFRPPPHNLEKKVVPFGADREKSLPSPKEDSDGAREPDSTVDLRKKNNKKKNYQ
RYAKPPYSYLAMISLVIQNSPEKRLKLSQILQDISSLFFFKGNYQGWKDSIRHNLSSNDCFRKV
LKDPLKPQAKGNYWTVDVTRIIPDALKLQNTAVTRQDLFPLDLAPYILHGQPYRSLERLSANHTR
GRTPRMEPEVQIPVSDPAVSFPMILWNLPTSYSKCVAPNVVAPPSIHPLLLYSNFPISINYNL
PPPYGSPVSDRRDLLASGLHPQIPLTPKPPPELKNAPSDFPNKTVDIPVYTGHPGFLASQSLF

SPHLPTATPPLVGYPSPGL

Figure 13

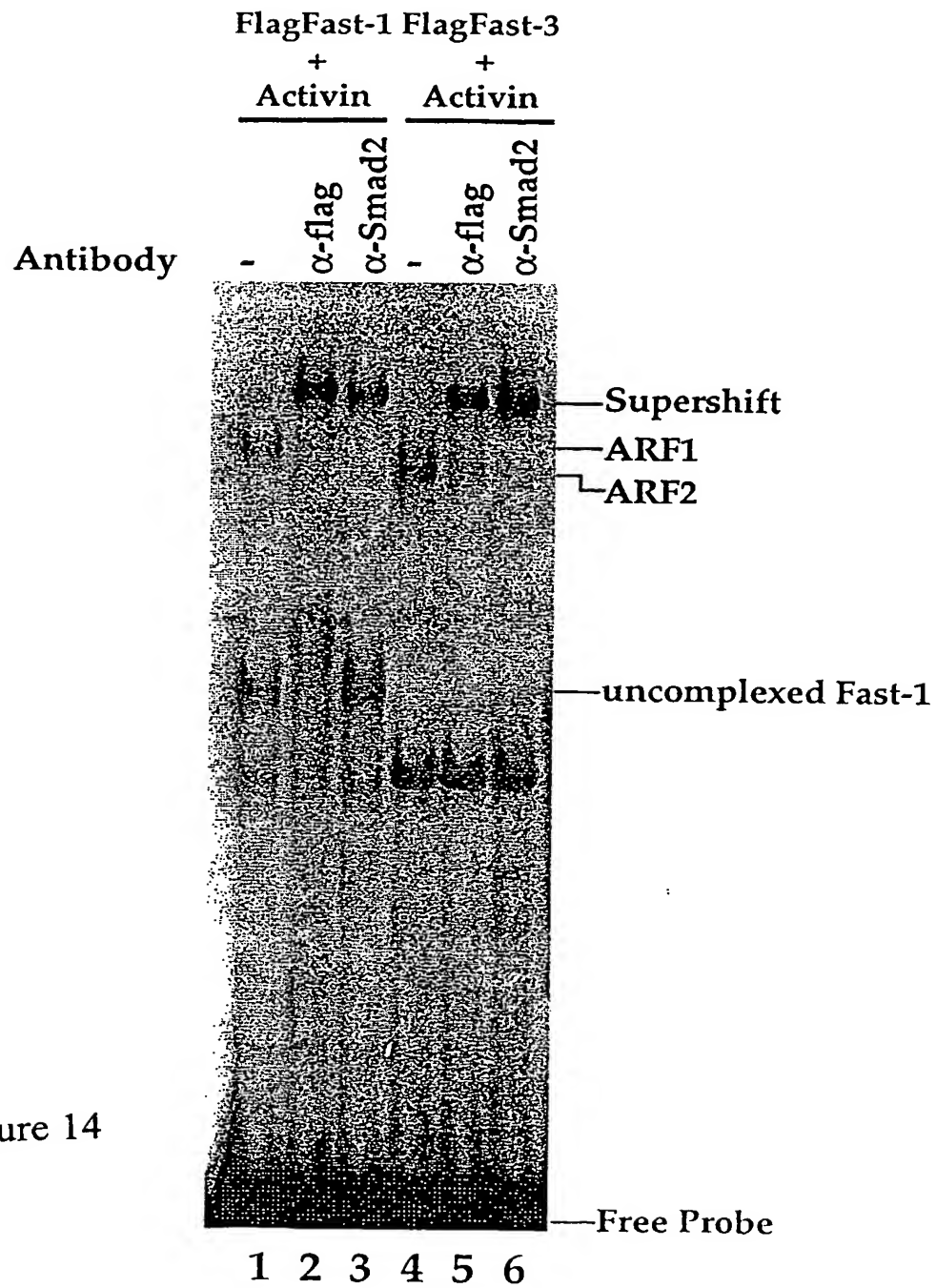


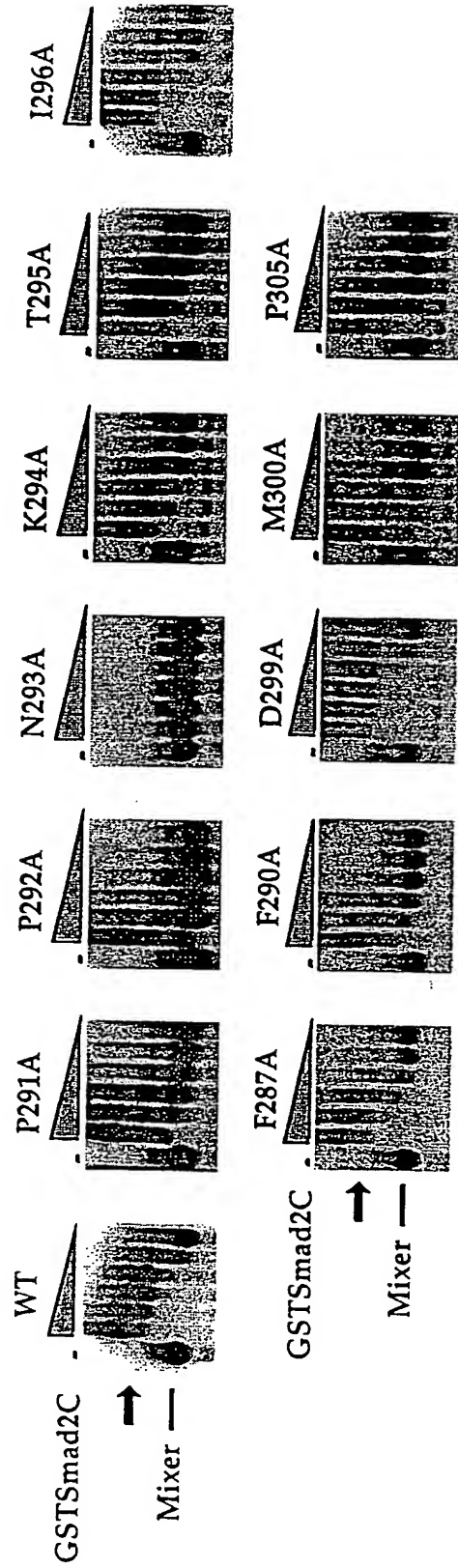
Figure 14

[illegible]

A Mixer SIM.

B

Single mutations



Double mutations

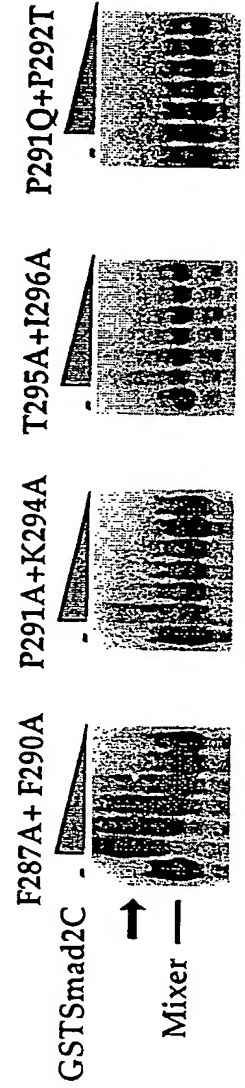
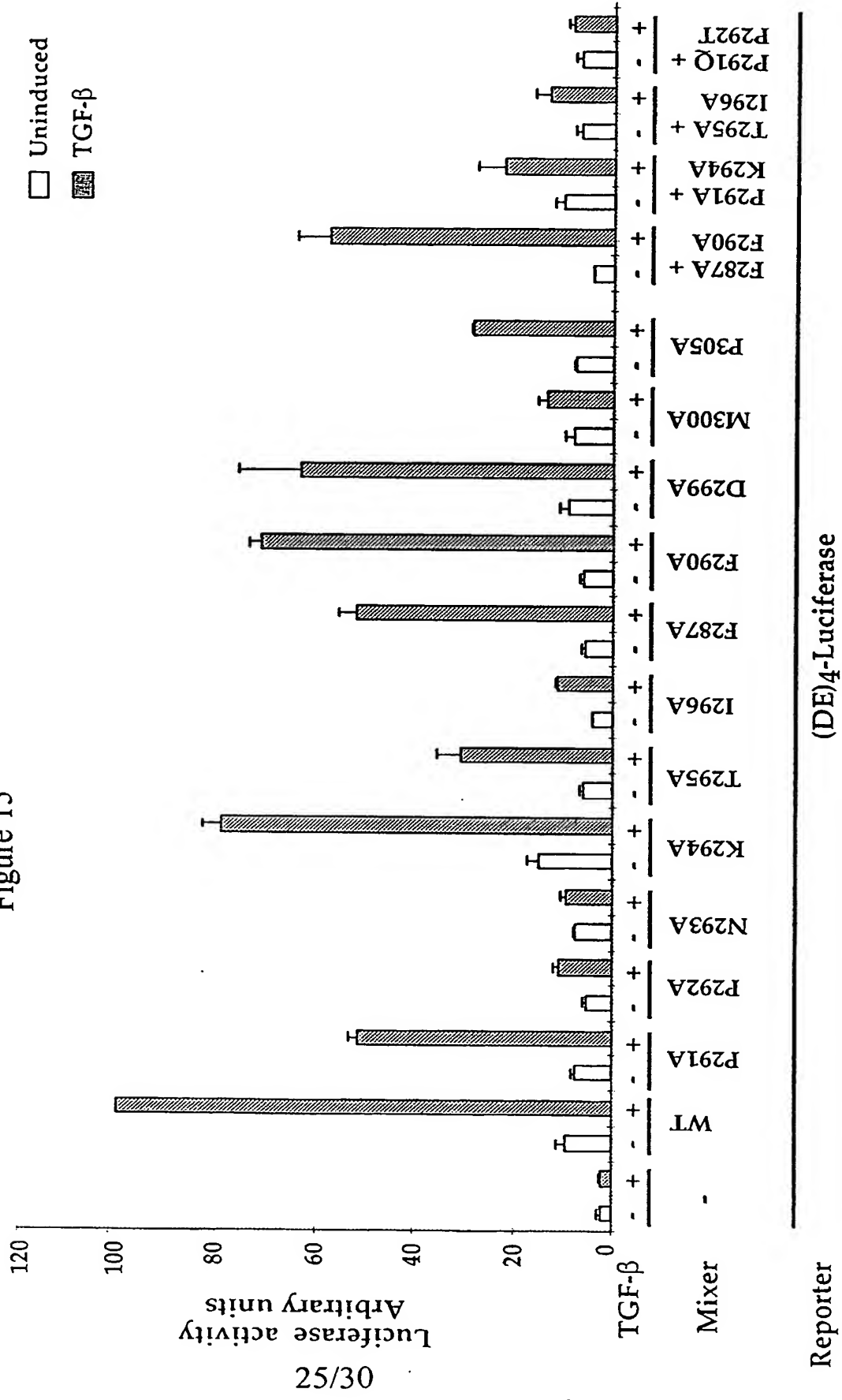


Figure 15

C

Figure 15



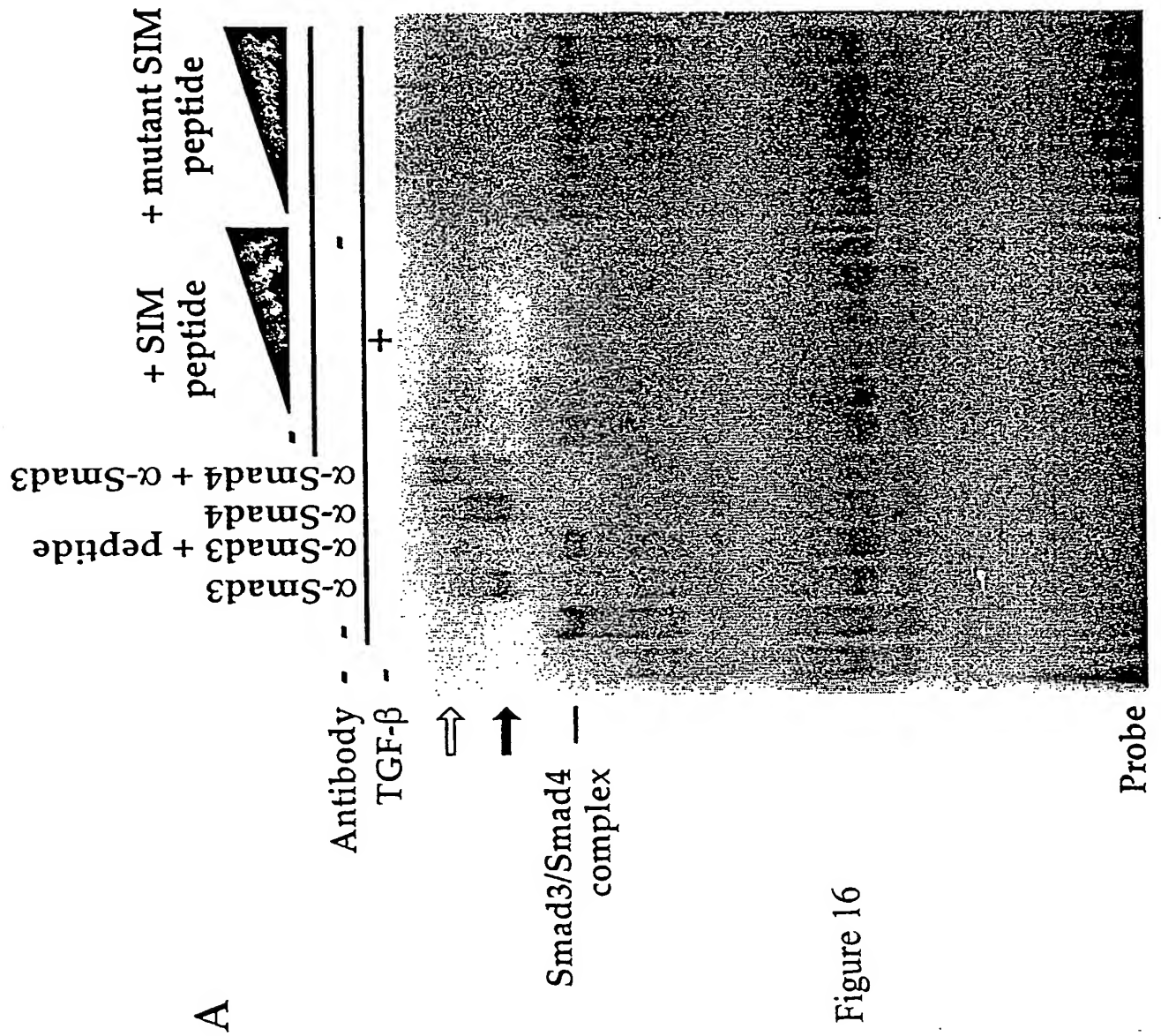


Figure 16

B

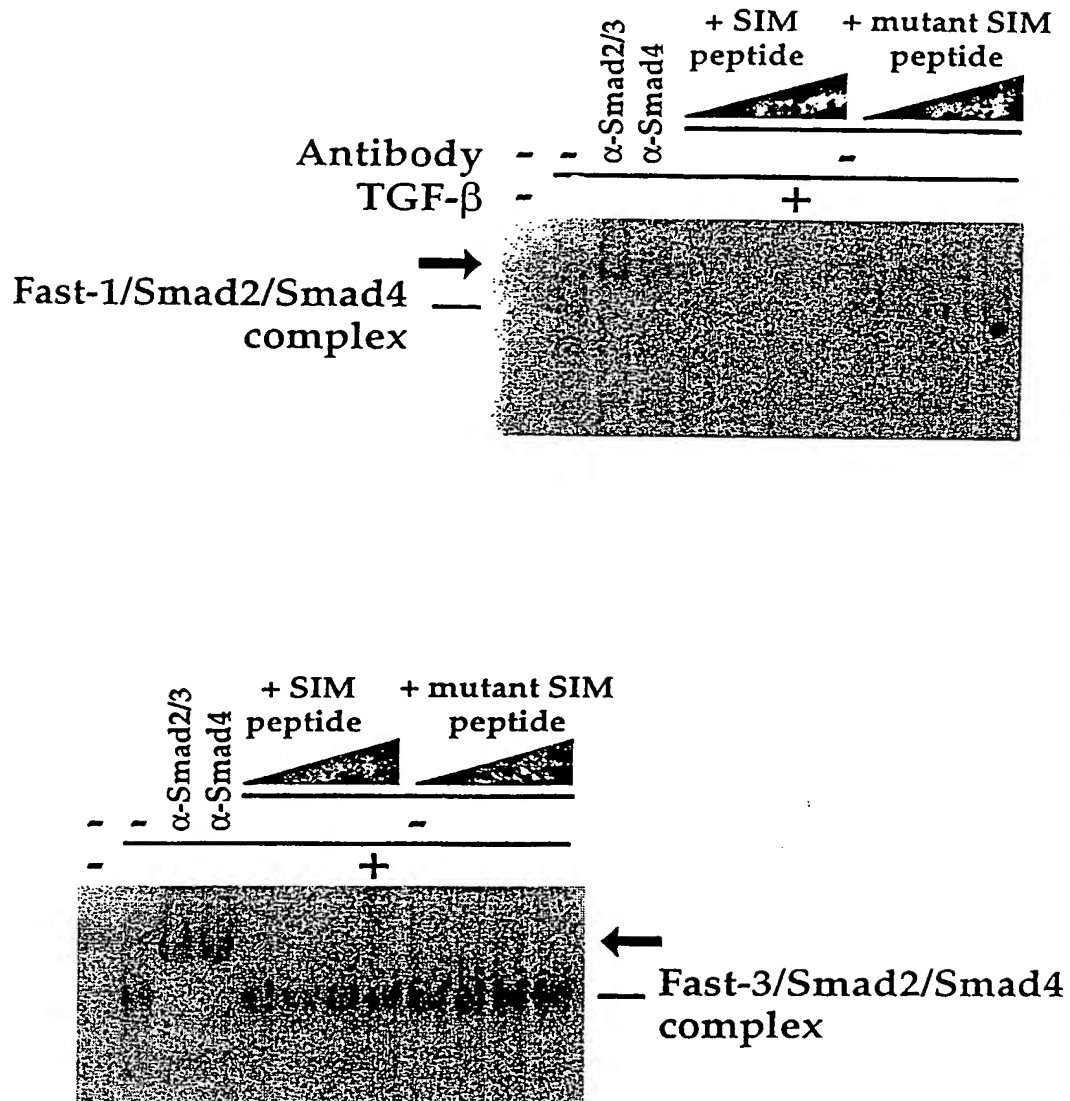


Figure 16

A

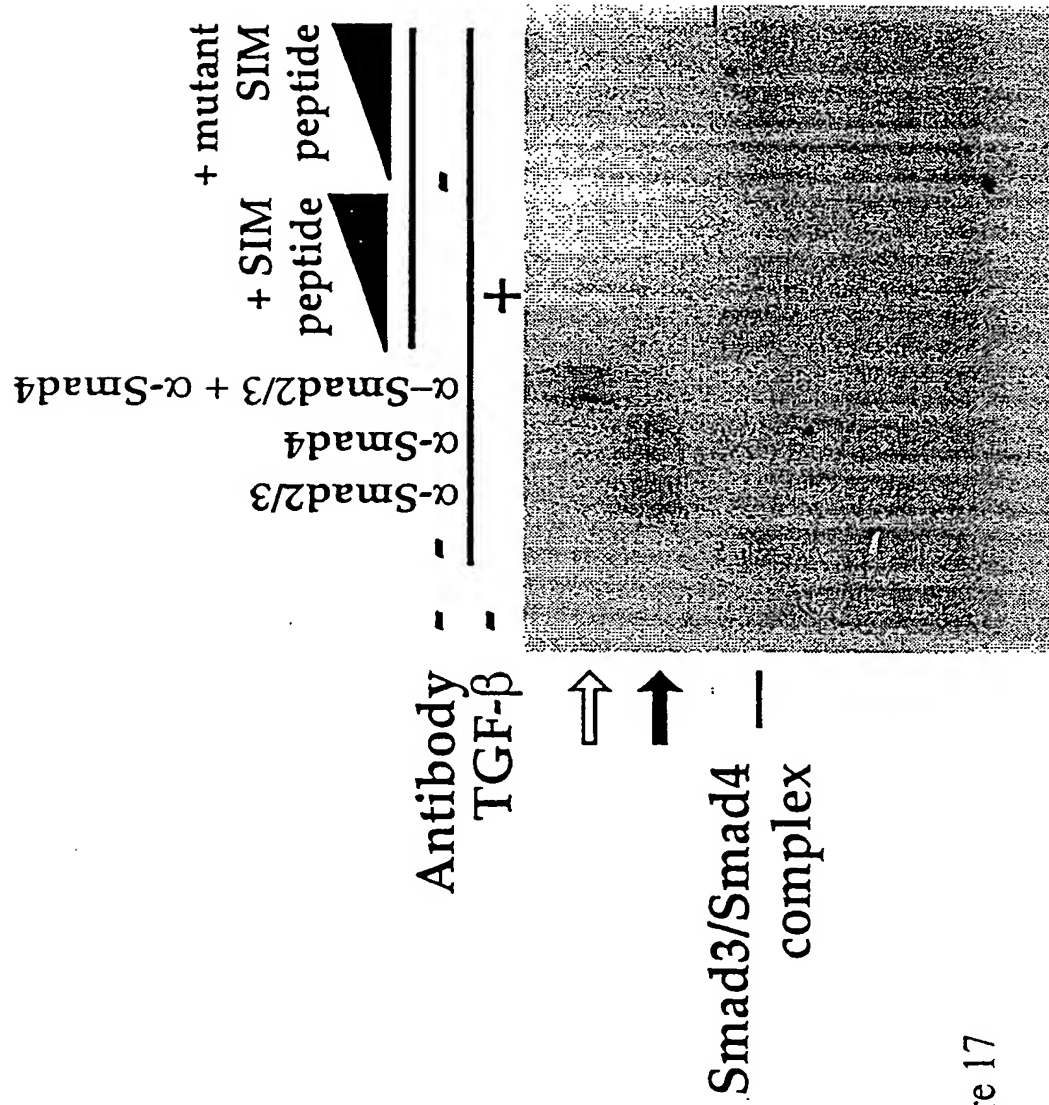
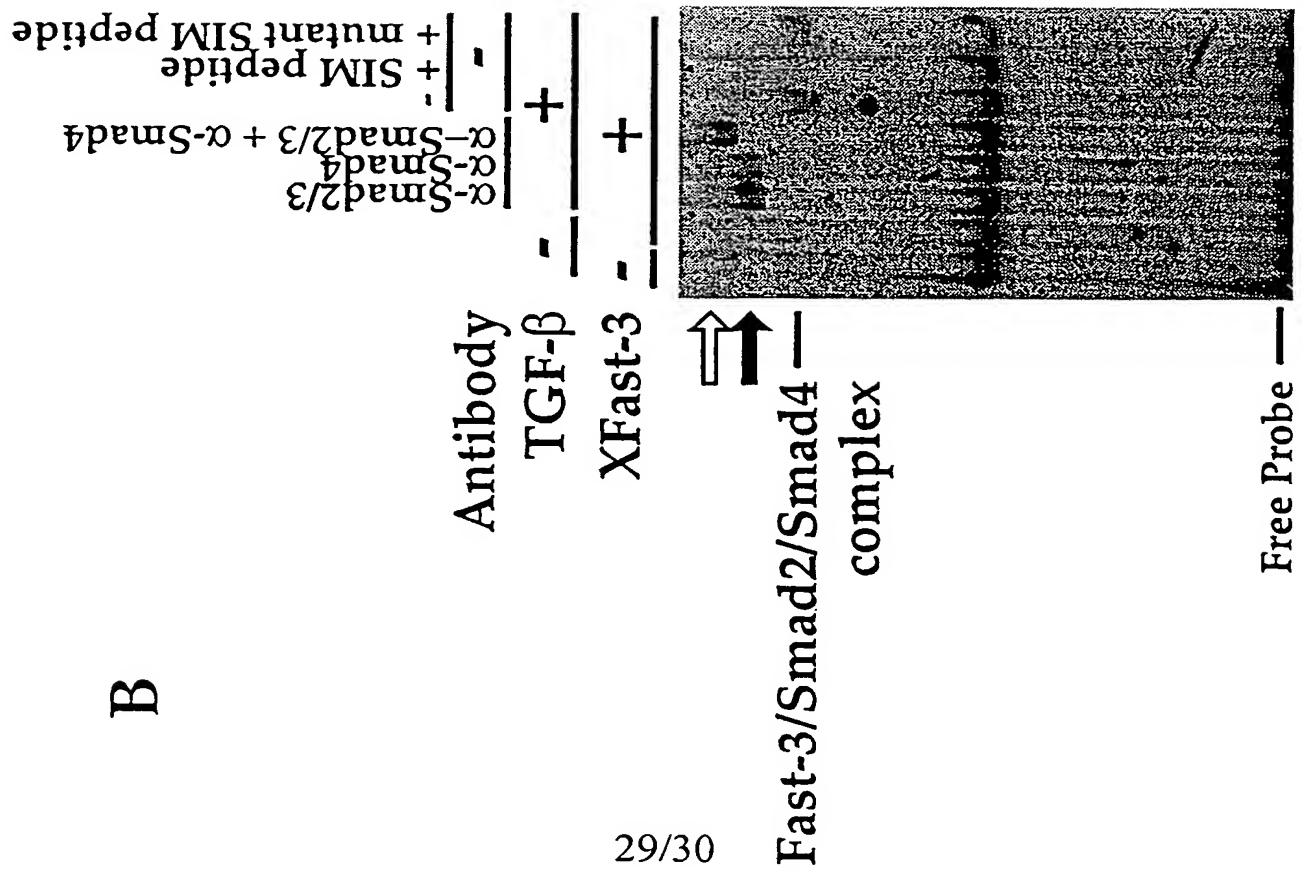


Figure 17



C

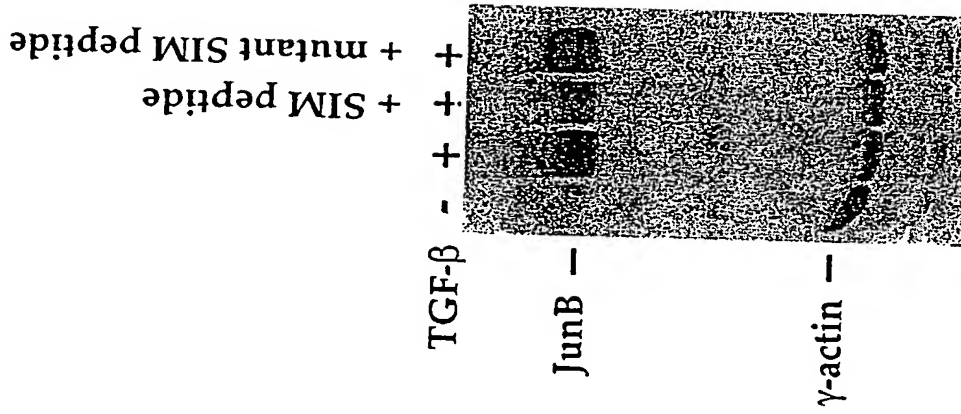


Figure 17

Figure 18

1 ATGTCTTTG GGCTTCACCC ATGGGATGTG GCCTTCAGAC CTTACACCCC
TCACAACCTG GAGAAGAAAG TCGTCCCCC AGGGCCGAC AGAGAGAAAT
101 CGCTTCCTTC CCCCAAGGAG GACAGTGATG GGGCCCGGA GCCCGACTCC
ACTGTGGATT TGAGGAAGAA GAACAAGAAG AAGAAGAACT ACCAGAGATA
201 CGCCAAGCCC CCTATTCCT ACCTGGCCAT GATCTCCCTG GTCATCCAGA
ACTCCCCCGA GAAGAGGCTC AACTCTCCC AGATCCTGCA GGACATCAGC
301 TCTCTGTTT CATTCITCAA GGGCAACTAC CAGGGCTGA AGGATCCAT
TCGGCATAAT TTGTCTTCCA ACGACTGTT CAGAAAGGTT CTGAAGGATC
401 CGCTCAAAGC ACAGGCCAAG GGCAATTACT GGACAGTAGA CGTGACCCGG
ATCCCCCCAG ACGCTTTGAA GCTCCAGAAC ACGGCGTGA CCCGGCAGGA
501 CCTGTTCCTT CTGGACCTGG CCCCCTACAT CCTACATGG CAGCCGTACA
GGAGTCTGGA GAGGCTCTCG GCCAATCACA CGAGGGGGCG CACGACCCCC
601 AGGATGGAGC CTGAAGTTCA GATTCCAGTG TCAGACCCAG CTGTCAGTTT
CCCCATGATC CTATGGAATC TGCCGACATC CTACAGCAA TGTGTGGCCC
701 CCAATGTAGT GGCCCCCTCCC AGCATTCACC CCTCTTGT GTACTCCAAC
TTCCCTTCCA TTTCATTTA TAACTACCTG CCCCCGCCCT ATGGCAGCCC
801 CGTGTAATCA GACAGACGAG ATCTTCTTGC CTCCGGCCTG CACCCCCAAA
TCCCTCTCAC CCCCAAACCC CCAGAGCTGA AGAACGCCCC CAGCGACTTC
901 CCCCCCAACA AGACAGTGTT TGACATCCCC GTCTATACTG GCCACCCGGG
GTTCCCTTGT AGCCAAAGCT TGTTCAGCCC ACACTTGCCC ACGGCTACAC
1001 CCCCCCTCGT GGGCTACCGG CCATCTGGC TATGA